1623
FB
7/31/02

COPY OF PAPERS
ORIGINALLY FILED

DOCKET NO.: ISIS-5037

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Achin H. Krotz, et al.

Serial No.: 10/103,906 **Group Art Unit: 1623**

Filing Date: March 22, 2002 **Examiner: Not Yet Assigned**

For: METHODS FOR REMOVING DIMETHOXYTRITYL GROUPS FROM OLIGONUCLEOTIDES

DATE OF DEPOSIT: 6/20/02
I HEREBY CERTIFY THAT THIS PAPER IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL, POSTAGE PREPAID ON THE DATE INDICATED ABOVE AND IS ADDRESSED TO THE ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, DC 20231.

TYPED NAME: Stephen C. Timmins
REGISTRATION NO.: 48,481

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

INFORMATION DISCLOSURE STATEMENT

Pursuant to 37 C.F.R. §1.56 and in accordance with 37 C.F.R. §§1.97-1.98, information relating to the above-identified application is hereby disclosed. Inclusion of information in this statement is not to be construed as an admission that this information is material as that term is defined in 37 C.F.R. §1.56(b).

☒ In accordance with §1.97(b), since this Information Disclosure Statement is being filed either within three months of the filing date of the above-identified application, within three months of the date of entry into the national stage of the above identified application as set forth in §1.491, before the mailing date of a first Office Action on the merits of the above-identified application, or before the mailing date of a first office action after the filing of request for continued examination under §1.114, no additional fee is required.

☐ In accordance with §1.129(a), this Information Disclosure Statement is being filed in connection with ☐the first or ☐second After Final Submission, therefore:

☐ Certification in Accordance with §1.97(e) is attached; or

☐ The fee of **$180.00** as set forth in §1.17(p) is attached.

☐ In accordance with §1.97(c), this Information Disclosure Statement is being filed after the period set forth in §1.97(b) above but before the mailing date of either a Final Action under §1.113 or a Notice of Allowance under §1.311, or before an action that otherwise closes prosecution in the application, therefore:

☐ Certification in Accordance with §1.97(e) is attached; or

☐ The fee of **$180.00** as set forth in §1.17(p) is attached.

☐ In accordance with §1.97(d), this Information Disclosure Statement is being filed after the mailing date of either a Final Action under §1.113 or a Notice of Allowance under §1.311 but before, or simultaneously with, the payment of the Issue Fee, therefore included are: Certification in Accordance with §1.97(e); and the submission fee of **$180.00** as set forth in §1.17(p).

☐ Copies of each of the references listed on the attached Form PTO-1449 are enclosed herewith.

☒ Copies of references listed on the attached Form PTO-1449 are enclosed herewith EXCEPT THAT:

☒ In view of the voluminous nature of references **33 and 34**, and the likelihood that these references are available to the Examiner, copies are not enclosed herewith.

☒ In accordance with §1.98(d), copies of the following references listed on the attached Form PTO-1449 are not enclosed herewith because they were previously cited by or submitted to the U.S. Patent and Trademark Office in patent application(s) for which a claim for priority under 35 U.S.C.§120 have been made in the instant application:

☒ Copies of references **1-49 and 51-53** listed on the attached Form PTO-1449 were previously cited by or submitted to the Patent and Trademark Office in prior application Serial No. **09/271,220**, filed **March 17, 1999** now issued as U.S. Patent No. **US 6,399,765 B1**, issued **June 4, 2002**.

☐ If any of the foregoing publications are not available to the Examiner, Applicant will endeavor to supply copies at the Examiner's request.

Please charge any deficiency or credit any overpayment to Deposit Account No. 23-3050. This form is submitted in duplicate.

There are no listed references which are not in the English language.

Date: 6/20/02

Stephen C. Timmins
Registration No. 48,481

WOODCOCK WASHBURN LLP
One Liberty Place - 46th Floor
Philadelphia, PA 19103
Telephone: (215) 568-3100
Facsimile: (215) 568-3439

COPY OF PAPERS
ORIGINALLY FILED

Form PTO-1449 Modified	Docket No. **ISIS-5037**	Serial No. **10/103,906**
List of Patent and Publications Cited by Applicant (Use several sheets if necessary)	Applicant **Achim H. Krotz et al.**	RECEIVED JUN 27 2002
U.S. Department of Commerce Patent and Trademark Office	Filing Date **March 22, 2002**	Group **1623** TECH CENTER 1600/2900

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)		
	1	Alul, R.H. et al., "Oxalyl-CPG: a labile support for synthesis of sensitive oligonucleotide derivatives", *Nucl. Acid Res.*, **1991**, *19*, 1527-1532
	2	Barber, I. et al., "Solution-Phase Synthesis of Phosphorothioate Oligodeoxynucleosides by the Phosphotriester Method," *Antisense Res. Devel.*, **1995**, *5*, 39-47
	3	Beaucage, S.L. et al., "Advances in the Synthesis of Oligonucleotides by the Phosphoramidite Approach", *Tetrahedron*, **1992**, *48*, 2223-2311
	4	Bonora, G.M. et al., "Large scale, liquid phase synthesis of oligonucleotides by the phosphoramidite approach," *Nucl. Acids Res.*, **1993**, *21(5)*, 1213-1217
	5	Chiang, M.Y. et al., "Antisense Oligonucleotides Inhibit Intercellular Adhesion Molecule 1 Expression by Two Distinct Mechanisms", *J. Biol. Chem.*, **1991**, *266*, 18162-18171
	6	Crooke, S.T. et al., "Pharmacokinetic Properties of Several Novel Oligonucleotide Analogs in mice", *J. Pharmacol. Exp. Therapeutics*, **1996**, *277*, 923-937
	7	Dahl, O. et al., "Preparation of Nucleoside Phosphorothioates, Phosphorodithioates and Related Compounds", *Sulfur Reports*, **1991**, *11(1)*, 167-192
	8	Eckstein, F., "Nucleoside Phosphorothioates", *Ann. Rev. Biochem.*, **1985**, *54*, 367-402
	9	Gait, M. J. ed., "An Introduction to Modern Methods of DNA Synthesis," *Oligonucleotide Synthesis, A Practical Approach*, IRL Press, Oxford, **1985**, IRL Press, Oxford, *Ch. 1*, 1-22
	10	Gebeyehu, G. et al., "Novel bitinylated nucleotide - analogs for labeling and colorimetric detection of DNA", *Nucl. Acids Res.*, **1987**, *15*, 4513-4534
	11	Kabanov, A.V.,"A new class of antivirals: antisense olgonucleotides combined with a hydrophobic substituent effectively inhibit influenza virus reproduction and synthesis of virus-specific proteins in MDCK cells", *FEBS Letts.*, **1990**, *259*, 327-330
	12	Kornberg, A., *DNA Replication*, W.H. Freeman and Co., San Francisco, **1980**, 75-77

EXAMINER	**DATE CONSIDERED**

Form PTO-1449 Modified	Docket No. ISIS-5037	Serial No. 10/103,906
List of Patent and Publications Cited by Applicant (Use several sheets if necessary)	Applicant **Achim H. Krotz et al.**	RECEIVED JUN 27 2002
U.S. Department of Commerce Patent and Trademark Office	Filing Date **March 22, 2002**	Group **1623** TECH CENTER 1600/2900

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	13	Kresse, J. et al., "The use of S-2-cyanoethyl phosphorothioate in the preparation of oligo 5'-deoxy-5'-thiothymidylates", *Nucl. Acids Res.*, **1975**, *2*, 1-9
	14	Letsinger, R.L. et al., "Cholesteryl-conjugated oligonucleotides: Synthesis, properties and activity as inhibitors of replication of human immunodeficiency virus in cell culture", *Proc. Natl. Acad. Sci.*, **1989**, *86*, 6553-6556
	15	Manoharan M. et al.,"Oligonucleotide Conjugates: Alteration of the Pharmacokinetic Properties of Antisense Agents", *Nucleosides and Nucleotides*, **1995**, *14*, 969-973
	16	Manoharan, M. et al., "Lipidic Nucleic Acids", *Tetrahedron Letts.*, **1995**, *36*, 3651-3654
	17	Manoharan M. et al., "Cholic Acid-Oligonucliotide Conjugates for Antisense Applications", *Bioorganic Med. Chem. Letts.*, **1994**, *4*, 1053-1060
	18	Manoharan, M. et al., "Introduction of a Lipophilic Thioether Tether in the Minor Groove of Nucleic Acids for Antisense Applications", *Bioorg. Med. Chem. Letts.*, **1993**, *3*, 2765-2770
	19	Manoharan, M. et al., "Chemical Modifications to Improve Uptake and Bioavailability of Antisense Oligonucleotides", *Annals NY Acad. Sciences*, **1992**, *660*, 306-309
	20	Martin, P., "Ein neuer Zugang zu 2'-O-Alkylribonucleosiden und Eigenschaften deren Oligonucleotide", *Helvetica Chemica Acta*, **1995**, *78*, 486-504
	21	Mishra, R.K. et al., "Improved leishmanicidal effect of phosphorotioate antisense oligonucleotides by LDL-medicated delivery", *Biochim. Et Biophysica*, **1995**, *1264*, 229-237
	22	Nielsen, P.E. et al., "Sequence-Selective Recognition of DNA by Strand Displacement with a Thymine-Substituted Polyamide", *Science*, **1991**, *254*, 1497-1500
	23	Oberhauser, B. et al., "Effective incorporation of 2'-O-methyl-oligonucleotides into liposomes and enhanced cell association through modification with thiocholesterol", *Nucl. Acids Res.*, **1992**, *20*, 533-538
	24	Padmapriya, A.A. et al., "Large-Scale Synthesis, Purification, and Analysis of Oligodeoxynucleotide Phosphorothioates," *Antisense Res. Devel.*, **1994**, *4*, 185-199

EXAMINER	**DATE CONSIDERED**

Form PTO-1449 Modified	Docket No. ISIS-5037	Serial No. 10/103,906
List of Patent and Publications Cited by Applicant (Use several sheets if necessary)	Applicant **Achim H. Krotz et al.**	
U.S. Department of Commerce Patent and Trademark Office	Filing Date **March 22, 2002**	Group **1623**

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	25	Paul, C.H. et al., "Acid binding and detritylation during oligonucleotide synthesis," *Nucl. Acids Res.*, **1996**, *24(15)*, 3048-3052
	26	Saison-Behmoaras, T. et al., "Short modified antisense oligonucleotides directed against Ha-*ras* point mutation induce selective cleavage of the mRNA and inhibit T24 cells proliferation", *EMBO J.*, **1991**, *10*, 1111-1118
	27	Sekine, M et al., "Synthesis and Properties of *S,S*-Diaryl Nucleoside Phosphorodithioates in Oligonucleotide Synthesis", *J. Org. Chem.*, **1979**, *44(13)*, 2325-2326
	28	Septak, M., "Kinetic studies on depurination and detritylation of CPG-bound intermediates during oligonucleotide synthesis," *Nucl. Acids Res.*, **1996**, *24(15)*, 3053-3058
	29	Shea, R.G. et al., "Synthesis, hybridization properties and antiviral activity of lipid-oligodeoxynucletide conjugates", *Nucl. Acids Res.*, **1990**, *18*, 3777-3783
	30	Svinarchuk, F.P. et al., "Inhibition of HIV proliferation in MT-4 cells by antisense oligonucleotide conjugated to lipophilic groups", *Biochimie*, **1993**, *79*, 49-54
	31	Wright, P. et al., "Large Scale Synthesis of Oligonucleotides via phosphoramidite Nucleosides and a High-loaded Polystyrene Support", *Tetrahedron Letts.*, **1993**, *34*, 3373-3376
	32	Yau, E.K. et al., "Synthesis of Dinucleoside and Dinucleotide Phosphorodithioates Via a Phosphotriester Approach", *Tetrahedron Letts.*, **1990**, *31(14)*, 1953-1956
*	33	Agrawal, S. (ed.), *Protocols for Oligonucleotides and Analogs*, Humana Press, Totowa, NJ, **1993**
*	34	Eckstein, F. (ed.), *Oligonucleotide and Analogues, A Practical Approach*, IRL Press, New York, **1991**

EXAMINER	DATE CONSIDERED

*A copy of these references will not be forwarded to the U.S. Patent and Trademark Office since they are believed to be too voluminous and easily obtainable by the Examiner.

Form PTO-1449 Modified	Docket No. ISIS-5037	Serial No. 10/103,906
List of Patent and Publications Cited by Applicant (Use several sheets if necessary)	Applicant **Achim H. Krotz et al.**	
U.S. Department of Commerce Patent and Trademark Office	Filing Date **March 22, 2002**	Group **1623**

U. S. PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Name	Class	Subclass
	35	4,415,732	11/15/83	Caruthers et al.	536	27
	36	4,458,066	07/03/84	Caruthers et al.	536	27
	37	4,500,707	02/19/85	Caruthers et al.	536	27
	38	4,517,338	05/14/85	Urdea et al.	525	54
	39	4,668,777	05/26/89	Caruthers et al.	536	27
	40	4,725,677	02/16/88	Köster et al.	536	27
	41	4,973,679	11/27/90	Caruthers et al.	536	27
	42	5,132,418	07/21/92	Caruthers et al.	536	27
	43	5,138,045	08/11/92	Cook et al.	536	27
	44	Re. 34,069	09/15/92	Köster et al.	536	27
	45	5,210,264	05/11/93	Yau	558	167
	46	5,218,105	06/08/93	Cook et al.	536	25.31
	47	5,459,255	10/17/95	Cook et al.	536	27.13
	48	5,539,082	07/23/96	Nielsen et al.	530	300
	49	5,571,902	11/05/96	Ravikumar et al.	536	22.1
	50	US 6,399,765 B1	06/04/02	Krotz, et a.	536	25.31

FOREIGN PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Country	Translation YES	Translation NO
	51	WO 92/20823	11/26/92	PCT		
	52	0035255 A1	09/1981	EPO		
	53	WO 96/03417	02/1996	PCT		

EXAMINER	DATE CONSIDERED